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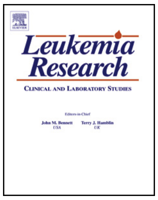

Adherence and future discontinuation of tyrosine kinase inhibitors in chronic phase chronic myeloid leukemia. A patient-based survey on 1133 patients

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ABSTRACT

Therapeutic approach for chronic myeloid leukemia (CML) patients has undergone a revolutionary change with the introduction of tyrosine kinase inhibitors, which improved overall survival and quality of life. Optimal therapy adherence has become of paramount importance to maximize the benefits in the long-term outcome. Several evidences have been reported that personal factors, such as social support, psychological and subjective perceptions about the drug used and the future, could influence adherence. We here report the results of a questionnaire specifically designed to evaluate factors influencing adherence and perceptions about the future, distributed to patients during regional Italian meetings. Overall, 1133 patients compiled the questionnaire: median age was 57 years. High rate of adherence was reported, but 42% of interviewed patients admitted that they had occasionally postponed a dose and 58% had discontinued therapy mainly for forgetfulness. The majority of patients discussed with personal physician about the importance of adherence and received sufficient information about illness and treatment, but would like to have discussed more about discomfort, anxiety and fear of the future. Summarizing personal drug compliance and estimating how many days a month, on average, the patients did not take the drug, the majority answered that it was less than 3 days (55%) and only a minority (4%) admitted that it was more than 7 days. Interviewed about discontinuation, 49% of patients answered that wouldn't interrupt because of fear of losing all the results achieved so far. This study suggests a higher level of satisfaction with more information received but the need of improving communication about possible future treatment free remission.

1. Introduction

Imatinib was the first molecular targeted therapy (i.e., tyrosine kinase inhibitors (TKIs) approved by the US Food and Drug administration (FDA) for chronic myeloid leukemia (CML) in early 2000. This drug dramatically improved CML patient outcomes by showing major clinical advantages and improved quality of life (QoL) compared to previous treatments, such as interferon (IFN) [1,2]. However, as imatinib or other TKIs are to be administered on a daily basis, maintenance of optimal QoL over the long-term period, has become a critical aspect of care in this cancer population. Some studies have shown that QoL of CML patients treated with imatinib is similar with that of their peers in the general population for patients aged 60 years or older, but major limitations exist for younger CML patients in several aspects of daily life activities [3].

Another key challenge introduced by the introduction of TKIs in the treatment of CML patients is that of adherence to therapy. Indeed, low adherence was shown to be associated to decreased rate of cytogenetic and molecular responses and, consequently, increased rate of progression and resistance [4,5]. Some studies have shown that a large proportion of CML patients do not fully adhere with treatment [4] and that this could be explained by both intentional and unintentional reasons [6]. However, patient adherence has been collected in different ways amongst the few studies conducted so far, thus hampering a clear understanding of factors associated with medication-taking behavior. This is also further complicated by the fact that, measuring adherence to therapy is challenging and all methods have “pro” and “cons” [7–9]. Also, the interplay between all the potential factors that can contribute to improve adherence in CML is poorly understood and more data are needed on this topic.

Therefore, as in the CML arena very few studies addressed this issue in the real-world setting [10,11] we have performed a large patient-based survey to investigate adherence behaviors and potential relationships with QoL, treatment satisfaction, and social life. Also, we focused on patient's attitude toward the possibility of drug discontinuation in future treatment free programs.

2. Patients and methods

In a series of meetings developed only for patients, an ad hoc survey including 25 items was designed and proposed. Patients were recruited from physicians from different centers on a specific invitation and therefore, based on the fact that were not selected, were representative of general CML population. The survey was designed based on real-life level of evidences and on literature review about adherence in CML. We included in the final analysis only questionnaires completely answered in each item. The items of the survey were grouped into the following board categories: (1) general questions about personal behavior; (2) relationship with treating physician; (3) perceptions of quality of life and adherence behaviors; (4) perceptions about future possible discontinuation of drug assumption. CML patients in treatment with any kind of TKI stemming from 30 Italian hematology centers: as some questions differed across centers, only the questions that were used in the majority of centers were analyzed. Overall, the analyzed questions from 28 centers were reported in this study: 13 centers from northern Italy, 7 from central Italy, 8 from southern Italy. Items included in the Survey are summarized in Appendix A.

In the final analysis were also considered the following features requested at the time of survey completion: gender, age, level of education and disease's duration. Descriptive statistics were provided for questions considering all the questions reported in at least 6 centers. Categorical variables (gender, education and all the questionnaire questions) were summarized by using frequency distributions (i.e. the number of patients in each level of the categorical variable) and percentages. Quantitative variables (age and disease duration) were summarized by using n, arithmetic mean, standard deviation, median, range, minimum and maximum.

3. Results

3.1. Population characteristics

Overall, 1133 patients completed the questionnaire, of them 658 males (58.1%) and 475 females (41.9%). Fifty-three percent of patients had a high level of education (high school-university), whereas 21% had only primary/elementary level and 25.7% a middle school level. Median age of patients was 57 years (range 17–90) and according to cumulative frequencies the most represented age category was that from 65 to 75 years (22.89%) followed by 55–65 years (21.72%) and 45–55 (19.75%). The majority of patients (79.55%) had a median duration of disease of less than 10 years.